

## Vitreoretinal Society of India practice pattern survey 2020: Medical retina

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**Purpose:** The aim of this study was to present the outcomes of the Vitreo-retinal Society of India (VRSI) Practice Pattern Survey 2020 in medical retina. **Methods:** An online survey of members of VRSI was conducted in April 2020 regarding their practice-patterns on varied medical and surgical retina topics concerning imaging and management approach. The results were evaluated by two independent experts in this field and compared with the evidence and other practice patterns in the world. **Results:** A total of 107 VRSI members participated in the online survey. Responses were obtained on management of wide-ranging chorioretinal disorders such as Central Serous Chorioretinopathy (CSCR), Polypoidal Choroidal Vasculopathy (PCV), Neovascular age related macular degeneration (n-AMD), Retinal Vein Occlusions (RVO), and Diabetic Retinopathy (DR). Participants were also surveyed regarding their attitudes and perceptions about anti-VEGF practice patterns and role of imaging in their current practice. Each of the survey question responses were then compared to contemporary literature, including evidence-based guidelines, randomized controlled trials (RCTs), real-world evidence and analogous international surveys. Comprehensive analysis related to this has been put forward in the article. **Conclusion:** This survey represents the contemporary practice patterns amongst vitreoretinal specialists in India. The survey results are vital for fellow practitioners to understand the 'standard of care' practice in medical retina. This will guide them to devise the best possible individualized treatment strategy for most favorable clinical outcomes.

**Key words:** As central serous chorioretinopathy, diabetic retinopathy, neovascular age related macular degeneration, polypoidal choroidal vasculopathy, practice patterns, retinal vein occlusions, vitreoretinal society of India

Over the past decades, we have witnessed significant advances in understanding the pathogenesis, diagnostics, and management of vitreoretinal diseases. This has improved our ability to provide better outcomes while treating these disorders. However, there have been numerous developments which have created controversies and challenges due to insufficient evidence, or complexity in interpreting the results, in both intervention and diagnostic imaging. Innovative technologies and interventions continue to progress rapidly while growing evidence base to support excellence in providing healthcare remains a mounting challenge.<sup>[1]</sup> Much of what is learnt and practiced today is based on data comprehended

from traditional randomized controlled trials (RCTs) and evidence-based guidelines.<sup>[1,2]</sup>

Although such forms of evidence-based system provide an excellent platform to formulate disease management protocol, their widespread application is challenging because they may not truly reflect the population diversities and the delivery settings in real-world practice.<sup>[2,3]</sup> To overcome this hurdle, researchers across the world are sharing their real-world evidence in varied patient population and clinical settings. Complementing this, certain retinal societies such as the American Society of Retina Specialists (ASRS) conduct their annual Preferences and Trends (PAT) Survey to evaluate the changing trends and practice pattern amongst different retina societies around the world, on a wide array of medical and surgical retina issues.<sup>[4]</sup>

Of late there has been considerable advocacy for assessing and sharing the best practice patterns amongst the Indian vitreo-retina specialists. In order to generate evidence regarding real-world preferred practice patterns in India, the Vitreo-retinal Society of India (VRSI) conducted an online survey in 2020. Questions were

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Received: 08-Aug-2020

Revision: 25-Jan-2021

Accepted: 26-Jan-2021

Published: 21-May-2021

### Access this article online

Website:

www.ijo.in

DOI:

10.4103/ijo.IJO\_2573\_20

### Quick Response Code:



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**Cite this article as:** Sheth JU, Gopal L, Gillies M, Khatri M, Kuppermann B, Roy R, *et al.* Vitreoretinal Society of India practice pattern survey 2020: Medical retina. Indian J Ophthalmol 2021;69:1430-9.

designed to address physician's perceptions and experiences on a varied range of medical and surgical retina topics. The objective of this manuscript is to present the outcomes of the 2020 VRSI Practice Pattern survey pertaining to medical retina.

## Methods

An electronic survey was sent to members of the VRSI in April 2020, and recipients were asked to complete the online survey within 15 days. The survey was collected using the Google forms and stored google sheets, which by default are encrypted. All the participants were identified. No ethical clearance was needed for the survey. The survey assessed members' practice patterns on a diverse range of medical and surgical retina topics. In the first part of the preferred practice pattern outcomes, we present the data in relation to the medical retina aspect. Questions were asked on important diseases on imaging, outcomes, and therapeutics. The questions were closed-ended, and participants were required to choose their response from the given options. There was no incentive or reward to complete the survey, and the survey was not sponsored by any third party. There were 28 questions and each question had 4-5 possible responses. Only one response was allowed to be selected in each question. The questionnaire is available as Supplemental Appendix 1.

The questions were structured and the options in the answers were given based on current literature available in that disease subject. The results of the survey were further analyzed by experts in medical retina (LG and MG). They provided a gap analysis of practice patterns in India versus major patterns in the world, such as the American PAT survey.

This was a cross-sectional, nonprobability sampling survey. The survey was delivered to 826 number of VRSI members by

email. This survey has a margin of  $\pm 8\%$  at 95% confidence level. Results are presented in the form of descriptive statistics and frequency tables. The responses are reported as nominal data that were analyzed using Excel (Microsoft, Richmond, USA).

## Results

### Central Serous Chorioretinopathy (CSCR)

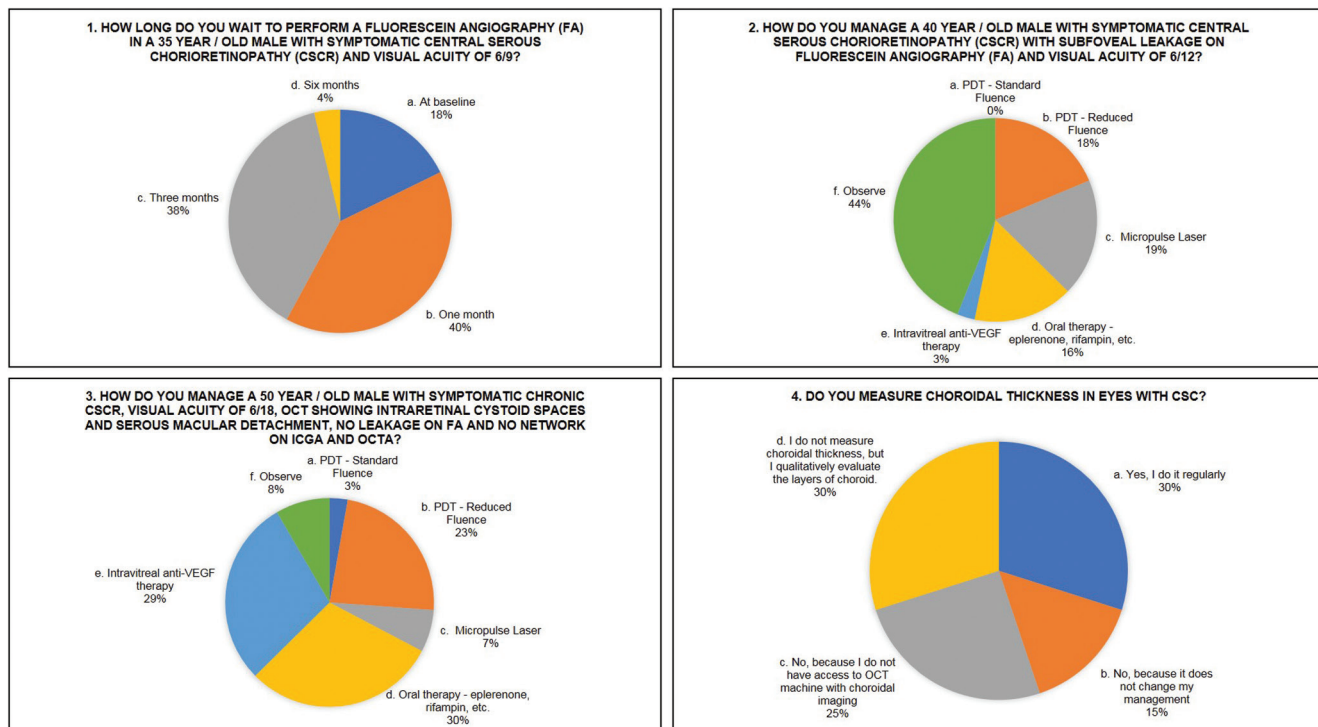
In a 35-year-old symptomatic man with fresh CSCR and visual acuity of 6/9, a similar number of respondents would wait at least 1 month (40%) or 3 months, respectively (38%) to perform a fluorescein angiography (FA) [Fig. 1; 1]. Interestingly, 18% of the respondents would perform FA at baseline in such a clinical scenario.

In total, 44% of respondents preferred to observe a 40-year-old symptomatic man with subfoveal leak, whereas an almost equal number of participants would perform a micropulse laser (19%) and a reduced fluence photodynamic therapy (RF-PDT; 18%), respectively, in such a patient [Fig. 1; 2].

Respondents were also asked their preferred management pattern in a 50-year-old symptomatic man with chronic CSCR without any leakage on FA. Similar proportions of respondents opted for oral therapy such as eplerenone, rifampicin, etc., (30%) and intravitreal anti-VEGF therapy (29%), whereas 23% of respondents chose to perform RF-PDT [Fig. 1; 3].

### Polypoidal Choroidal Vasculopathy (PCV)

For a subfoveal PCV, almost half of the respondents (47%) would start with anti-VEGF monotherapy and switch to PDT if there is no response after three injections, whereas only 12% opted to perform a combination of PDT + anti-VEGF injection at baseline [Fig. 2; 5].



**Figure 1:** Practice pattern survey data pertaining to central serous chorioretinopathy (CSCR) and its management

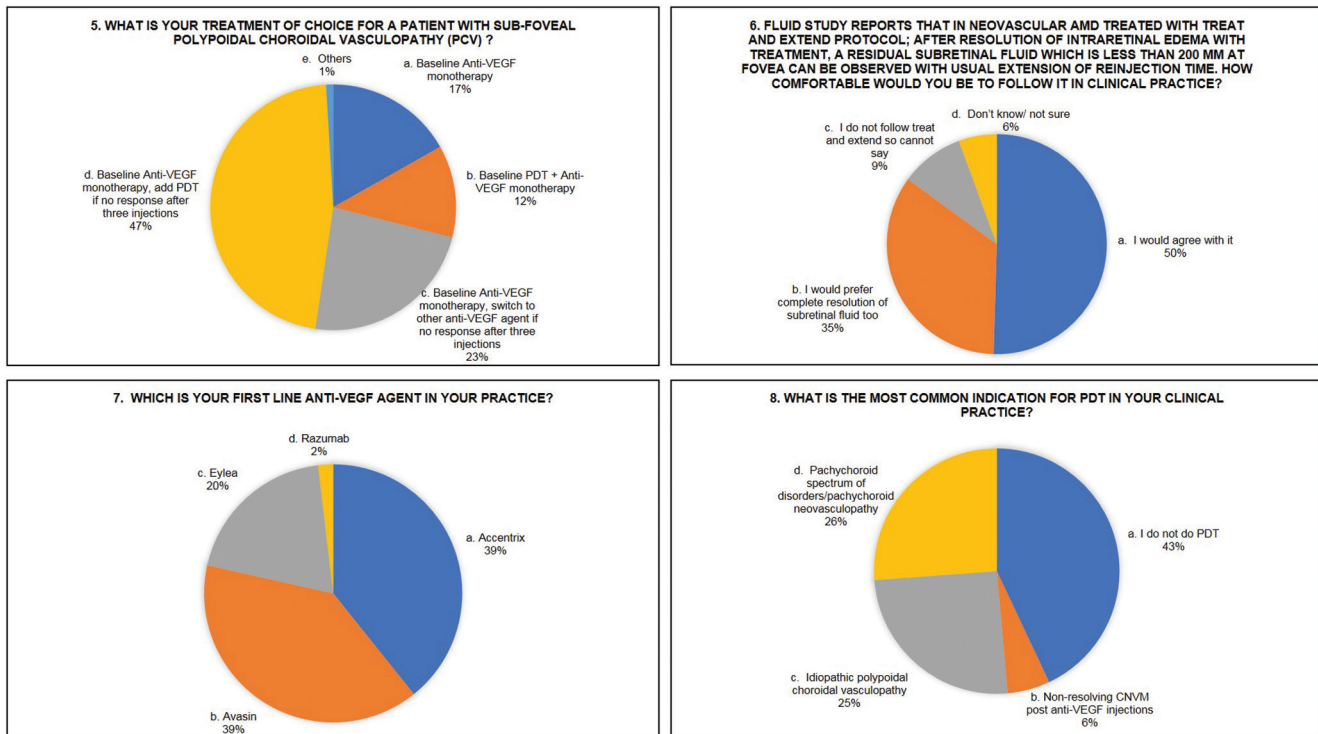


Figure 2: Practice pattern survey data pertaining to choroidal neovascular membrane (CNVM) and its management

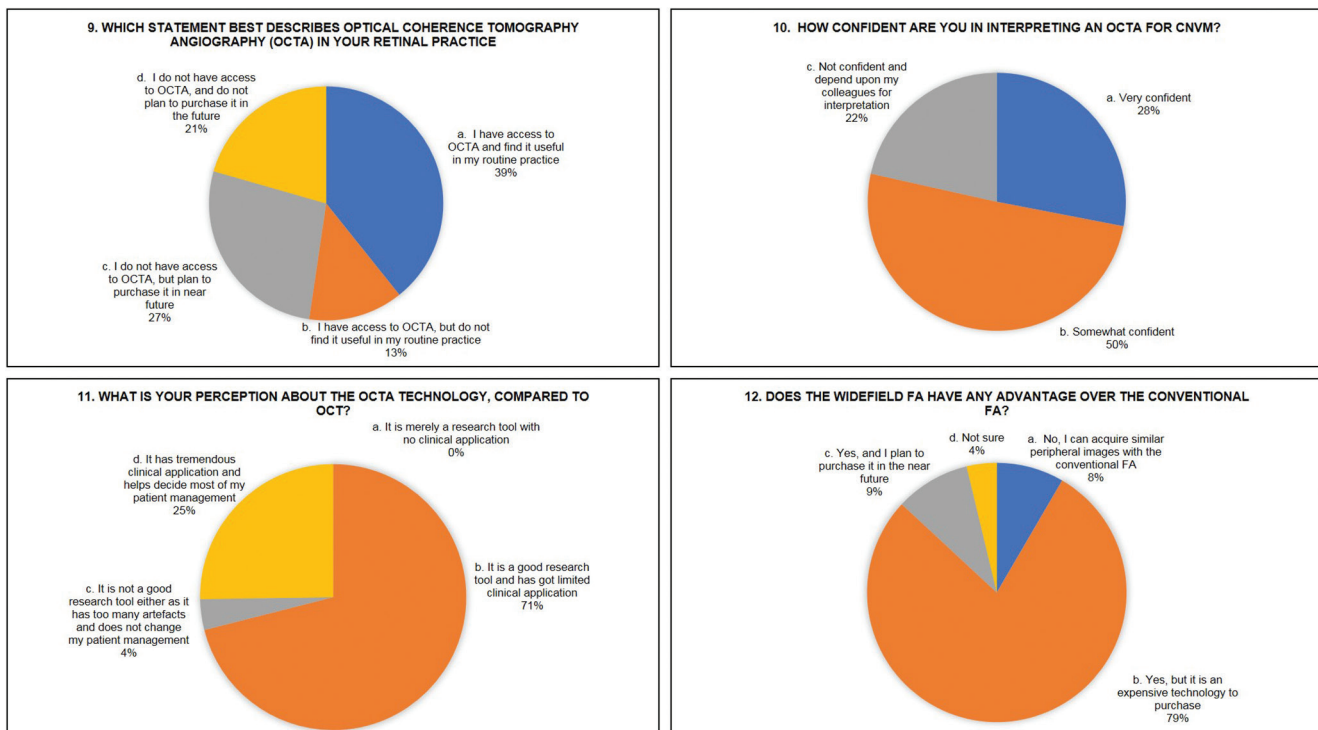


Figure 3: Practice pattern survey data pertaining to chorioretinal imaging

When the participants were questioned regarding the common indications for performing PDT in their clinical practice, the commonest indication were pachychoroid disease spectrum/pachychoroid neovascuopathy (PNV; 26%),

idiopathic PCV (25%) and nonresolving choroidal neovascular membrane (CNVM) post anti-VEGF injections (6%). Remarkably, 43% of the participants responded that they do not perform PDT at all [Fig. 2; 8].



### Neovascular age related macular degeneration (n-AMD)

More than half of the respondents (50%) were willing to tolerate sub-retinal fluid (SRF) less than 200  $\mu\text{m}$ , whereas one-third of them (35%) preferred complete resolution of SRF in management of n-AMD [Fig. 2; 6].

### Imaging

In CSCR, 30% of respondents measure the choroidal thickness (CT) regularly, whereas an equivalent number of participants qualitatively evaluate the layers of choroid, although not measuring the CT. Notably, one-fourth of respondents (25%) do not measure the CT as they do not have access to OCT machines with choroidal imaging [Fig. 1; 4].

More than half of the participants (52%) have access to optical coherence tomography angiography (OCTA) and 39% of them find it useful in their routine practice [Fig. 3; 9]. Additionally, 27% of participants do not have access to OCTA, but plan to purchase it in near future. When the respondents were asked regarding their proficiency in interpreting OCTA for CNVM, 28% were very confident and 50% of them were somewhat confident, whereas 22% were not confident and depended upon their colleagues for interpretation [Fig. 3; 10]. Regarding their perception of OCTA technology, a majority of the participants (71%) felt that it is a good research tool with limited clinical application. In contrast, a quarter of them (25%) deemed it to have tremendous clinical application and helps to decide most of their patient management [Fig. 3; 11].

A bulk of the participants considered widefield FA as advantageous over the conventional FA, but at the same time noted it to be an expensive technology to purchase (79%). Only a small number of them felt that both technologies are comparable, and they can acquire similar peripheral images with the conventional FA (8%) [Fig. 3; 12].

### Retinal Vein Occlusions (RVO)

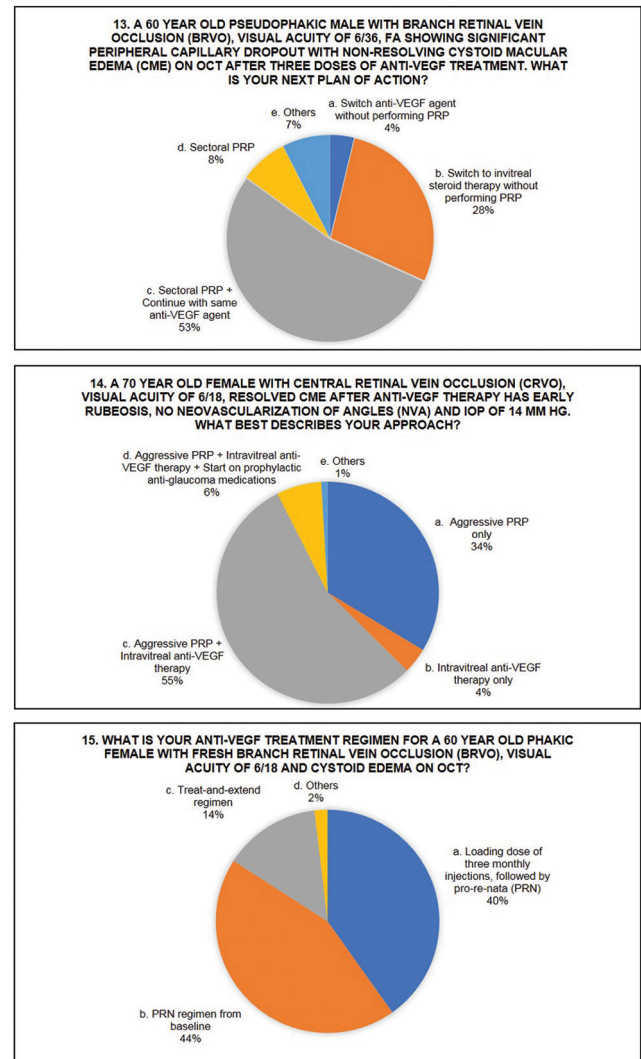
In a case of 60-year-old pseudophakic man having branch retinal vein occlusion (BRVO) with nonresolving cystoid macular edema (CME) after three anti-VEGF injections and significant peripheral capillary dropout on FA, more than half of the participants would add sectoral pan-retinal photocoagulation (PRP) to the same anti-VEGF injection (53%), whereas 28% of participants would prefer switching to intravitreal steroids without performing PRP. Only 4% of the participants would switch the anti-VEGF agent without adding PRP [Fig. 4; 13].

For management of a 70-year-old woman with central retinal vein occlusion (CRVO) and resolved CME with early rubeosis and normal intraocular pressure (IOP; 14 mm Hg), 55% would perform aggressive PRP with intravitreal anti-VEGF therapy whereas 34% would perform aggressive PRP only. 6% of them would also prophylactically add anti-glaucoma medications to aggressive PRP with intravitreal anti-VEGF therapy [Fig. 4; 14].

In choosing an anti-VEGF treatment regimen for a 60-year-old woman with fresh BRVO with CME, we noted similar number of respondents selecting pro-re-nata (PRN) regimen from baseline (44%) and a regimen having loading doses of three monthly injections followed by PRN (40%) [Fig. 4; 15].

### Diabetic Retinopathy (DR)

When the participants were presented with a clinical scenario of a 35-year-old type 1 diabetic man with early



**Figure 4:** Practice pattern survey data pertaining to retinal vein occlusions (RVO) and their management

proliferative diabetic retinopathy (PDR) in OD and very severe nonproliferative diabetic retinopathy (NPDR) in OS with a dry macula in both eyes, the most common line of management chosen was performing PRP in both eyes (59%), followed by OD PRP and OS observation (29%), both eyes PRP with both eyes anti-VEGF injections (6%), both eyes PRP with OD anti-VEGF injection (4%) and OD PRP + anti-VEGF injection with OS observation (2%), respectively [Fig. 5; 16].

In a 54-year-old diabetic patient with moderate NPDR changes and center-involving diabetic macular edema (ci-DME) of 370  $\mu\text{m}$  and HbA1c level of 8.3%, a majority of respondents (62%) would advise good glycemic control with topical nonsteroidal anti-inflammatory drug (NSAID) drops and repeat optical coherence tomography (OCT) after 4–6 weeks, whereas only 8% of them would advise intravitreal anti-VEGF therapy [Fig. 5; 17].

In DME management, 68% of participants perform macular laser along with anti-VEGF therapy only when the edema is nonresolving after three anti-VEGF injections. A very small section of the participants (8%) do not perform macular laser in the management of DME [Fig. 5; 18].

In a patient with ci-DME and visual acuity of 6/18, the anti-VEGF agent of choice was Ranibizumab (47%) followed by Bevacizumab (27%), the Ranibizumab biosimilar Razumab (20%), Aflibercept (5%) and Ziv-aflibercept (1%), respectively [Fig. 6; 20].

Although protocol-T concluded that aflibercept led to a greater number of letters gained in eyes with poor initial visual acuity and also had less thromboembolic events in DME, only 13% of respondents preferred to use it over ranibizumab or bevacizumab in eyes with poor initial vision [Fig. 6; 21]. Majority of them (61%) still chose to start with Ranibizumab or Bevacizumab, and switch to Aflibercept only if there is poor response.

For a nonresponsive DME, when the participants were asked after how many injections do they switch, more than half responded that they would do so after three injections (56%), followed by 1-2 injections (15%) and 4-6 injections (12%), respectively [Fig. 6; 22]. 17% of respondents said that they do not switch between anti-VEGF injections. Additionally, in a pseudophakic patient with DME, unresponsive to three doses of anti-VEGF agents, more than half of the respondents would prefer switching to intravitreal steroids (54%) [Fig. 6; 23]. This response was followed by other management options including focal laser with intravitreal steroids (28%), focal laser with anti-VEGF agent (7%), switching to other anti-VEGF agents (6%) and others (5%), respectively.

In DME follow-up of a patient on long-standing anti-VEGF injection therapy, 57% of respondents noted that they would perform clinical examinations at all visits and advise OCT when needed (57%), whereas 41% respondents said that they would perform clinical examination with OCT at all visits [Fig. 7; 24]. Only 2% of respondents said that they perform OCT at all visits without clinical examination.

Half of the participants (50%) would prefer starting the patient of DME on intravitreal steroids if they are pseudophakic and/or with a recent history of thromboembolic events [Fig. 7; 26]. Notably, 31% of participants do not start with intravitreal steroids unless there is a history of recent thromboembolic events. When the participants were asked regarding the duration of efficacy of intravitreal dexamethasone implant (Ozurdex) in DME, majority felt that it lasted for 3 months (60%), followed by 2 months (19%), 4 months (16%) and 6 months (5%), respectively [Fig. 7; 27]. Besides, when the participants were questioned regarding the management of a 70-year-old phakic patient with DME and recent history of stroke, 59% would immediately start with an intravitreal steroid [Fig. 7; 25]. At the same time, 19% would wait for 2-3 months and 11% of respondents would wait 1 month and >6 months each to give anti-VEGF therapy in such patients.

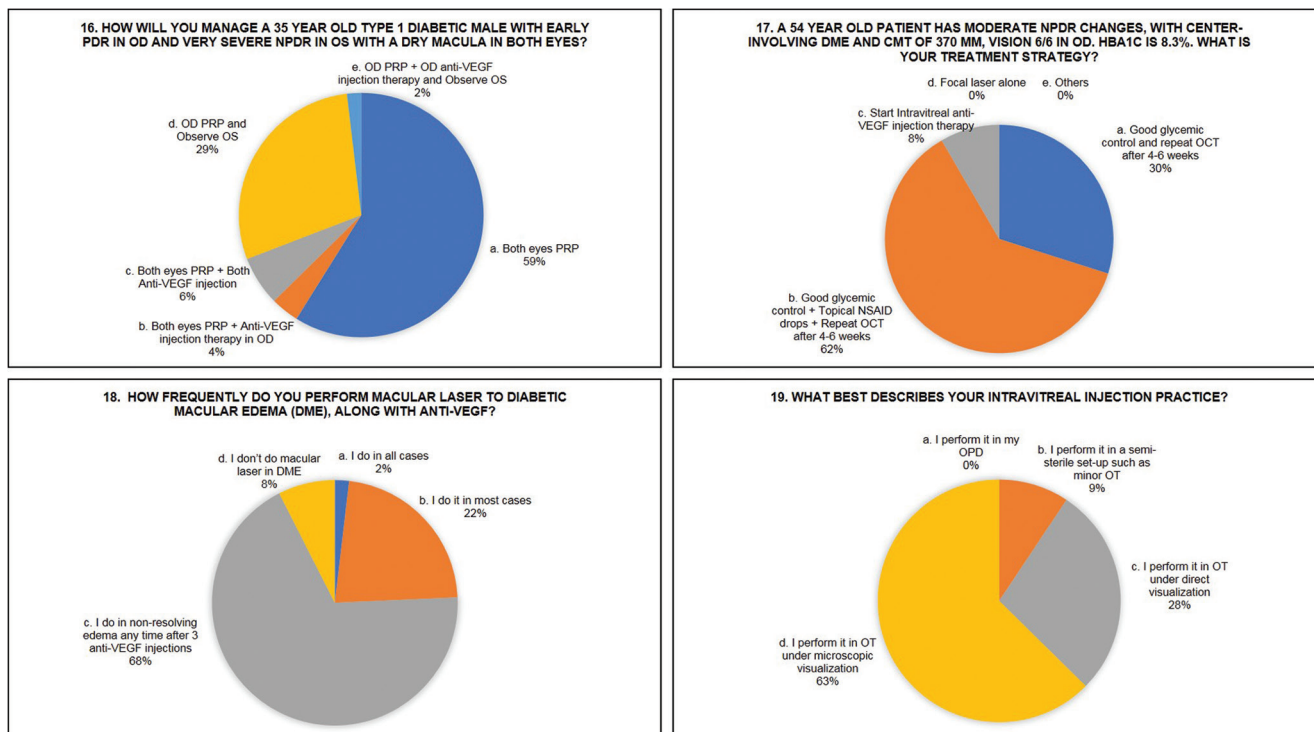
**Anti-VEGF therapy**

An equal number of participants (39%) chose Ranibizumab and Bevacizumab as the first line of anti-VEGF agent in their clinical practice, followed by the ranibizumab biosimilar Razumab (20%) and Aflibercept (2%), respectively [Fig. 2; 7].

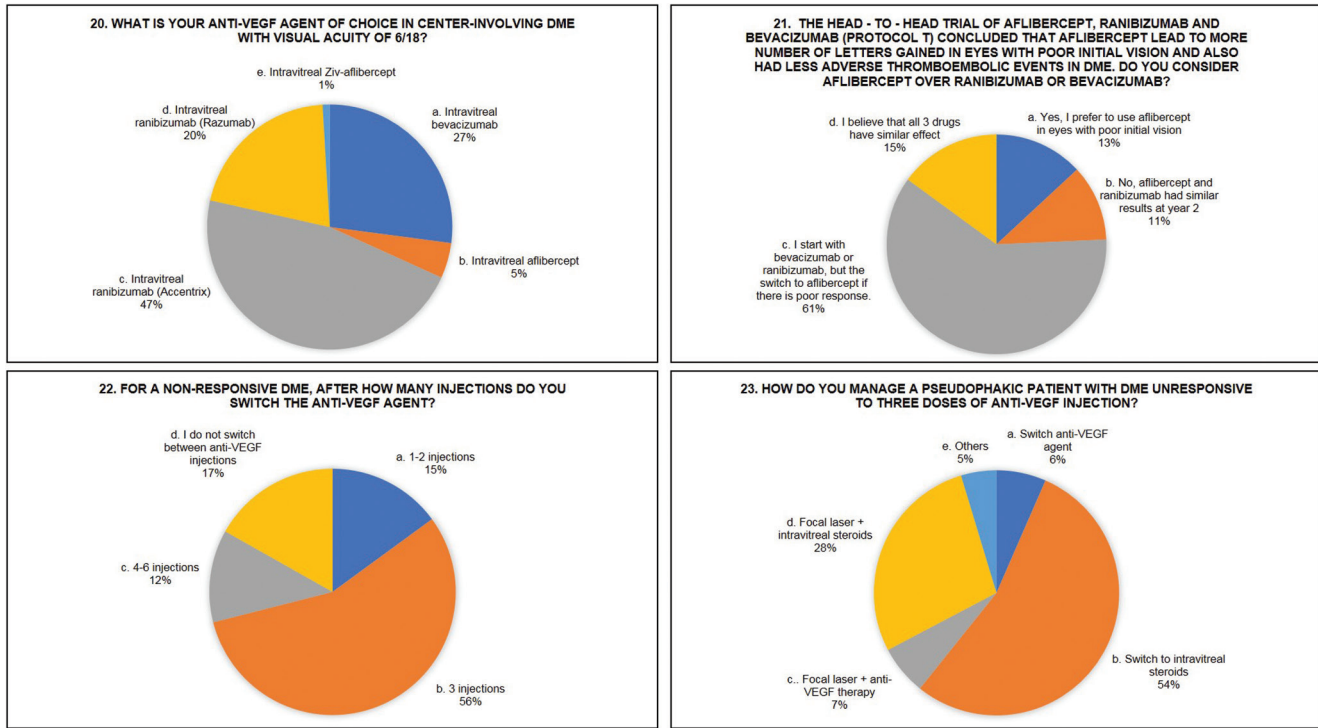
Regarding intravitreal injection practice, 63% of participants responded that they perform it in the operation theater (OT) under microscopic visualization, followed by 28% who performed in OT under direct visualization and 9% performed it in a semi-sterile setup such as minor OT [Fig. 5; 19].

**Discussion**

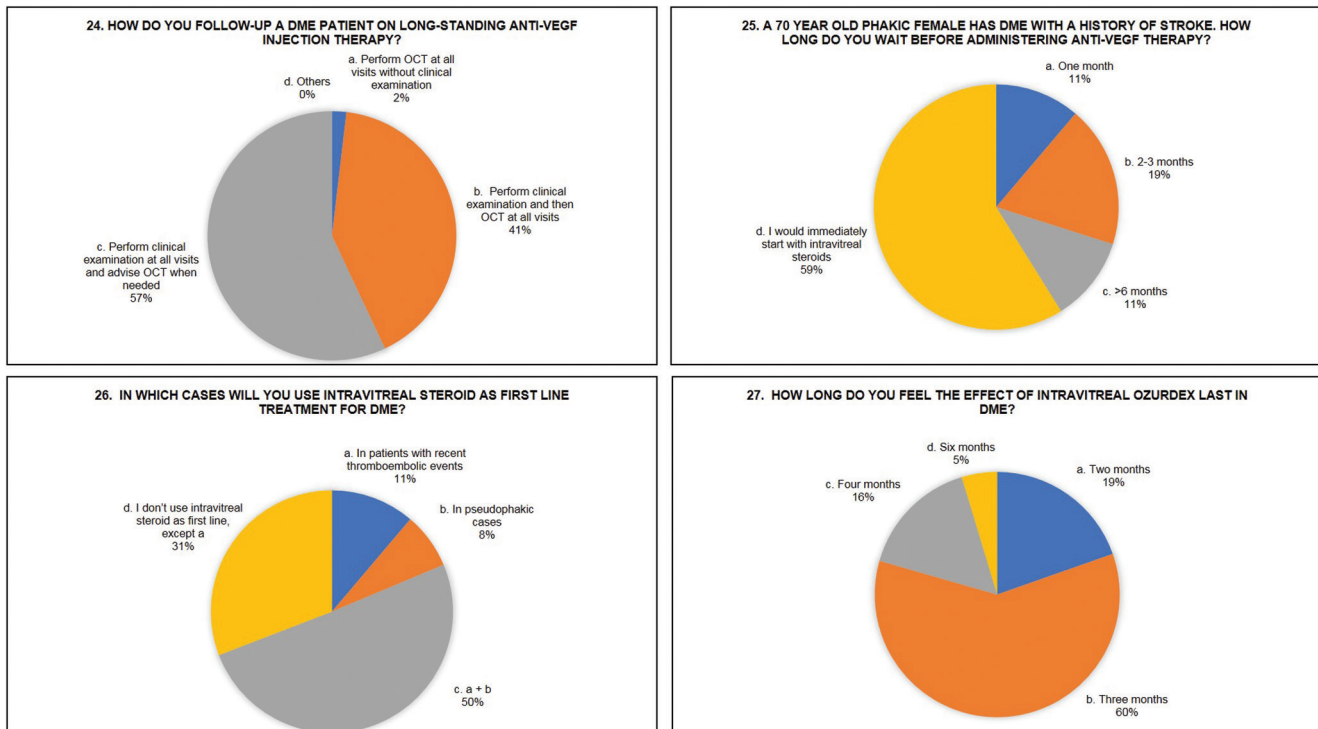
Acute CSCR is known to have good visual prognosis and usually resolves within 3-4 months without treatment.<sup>[5,6]</sup> In our survey, most Indian retina specialists also preferred to



**Figure 5:** Practice pattern survey data pertaining to diabetic retinopathy (DR) and its management



**Figure 6:** Practice pattern survey data pertaining to intravitreal anti-vascular endothelial growth factor (anti-VEGF) therapy for management of fresh diabetic macular edema (DME) and nonresponsive DME



**Figure 7:** Practice pattern survey data pertaining to intravitreal steroid therapy for management of diabetic macular edema (DME) and follow-up of patients with DME

wait for a least 1 (40.2%)–3 (38.3%) months to perform FA in a case of acute CSCR. A small number of respondents (18.7%)

also preferred to perform RF-PDT and Micropulse laser, respectively, for CSCR with subfoveal leakage. Following



the treatment, the choroidal thickness and the vascular diameter have been shown to reduce significantly.<sup>[7,8]</sup> Our survey results indicated that evaluation of choroid is usually performed by the participants, either by measuring the choroidal thickness (29.9%) or by assessing the choroidal morphology (29.9%), respectively.

Stattin *et al.* have shown that reduced fluence PDT is an is a safe and considerable treatment option in acute CSCR.<sup>[9]</sup> Micropulse laser causes negligible thermal damage to the retina, thereby making it suitable for application in subfoveal leak.<sup>[10]</sup> For chronic CSCR, PDT has been shown to be superior to subthreshold laser in the resolution of subretinal fluid and functional outcomes.<sup>[11]</sup> We noticed a similar trend in our survey, where the participants chose to perform RF-PDT (23.4%) over Micropulse laser (6.5%) in the management of chronic CSCR. Interestingly, more participants were willing to perform intravitreal anti-VEGF therapy (29%) or give oral therapy such as eplerenone, rifampicin, etc., (29.9%) in chronic CSCR. This could be due to the limited availability of micropulse laser and PDT. Meta-analysis has shown that anti-VEGF may not have much role in management of acute CSCR but it is a viable treatment option in chronic CSCR.<sup>[12,13]</sup> Likewise, the ambiguity of CSCR pathogenesis has led to an advent of wide variety of oral therapeutic agents been tried in its management. Possible role of endogenous mineralocorticoid dysfunction has paved way for use of agents such as eplerenone, rifampicin, and spironolactone.<sup>[14]</sup>

In PCV, whereas the Everest II study showed better results with combination of Ranibizumab with verteporfin PDT, the Planet study has shown that monotherapy with Aflibercept is not inferior to combination of Aflibercept with rescue PDT.<sup>[15,16]</sup> Almost half of the participants (46.7%) in the survey preferred to treat a subfoveal PCV with anti-VEGF monotherapy and then switch to PDT if there is no response after three injections whereas only 12.1% preferred to start with a combination therapy of PDT + intravitreal anti-VEGF. Cost-effectiveness could be one of the reasons to favor such a line of management. Doble *et al.* have shown that combination therapy (PDT + Intravitreal Ranibizumab) is more effective and less costly than Ranibizumab monotherapy during a lifetime horizon.<sup>[17]</sup> However, if the time horizon was reduced to less than 10 years and/or reduction in cost of monotherapy was done, then combination therapy was no longer cost-effective.

The FLUID study showed that patients who received intravitreal Ranibizumab by treat-and-extend protocol and who tolerated a sub-retinal fluid levels of <200  $\mu$ m achieved a visual acuity that was comparable, with fewer injections, with that achieved when treatment was intended to resolve all SRF completely.<sup>[18]</sup> A similar clinical scenario was presented in the survey and we found that 50.5% of the respondents were willing to tolerate SRF, whereas 34.6% preferred complete resolution of SRF.

OCTA is a noninvasive imaging modality to visualize the retinal and choroidal blood vessels.<sup>[19]</sup> In the 2019 ASRS PAT survey, 46% of the respondents had access to OCTA, whereas only 27.1% found it useful in their clinical practice.<sup>[20]</sup> Concurrently, in the VRSI survey, we observed marginally higher numbers of retinal specialists with access to OCTA technology (52.4%) and found it useful in their routine practice (39.3%). Additionally, almost 71% of the participants

consider it to be a good research tool with limited clinical application, whereas a quarter of them (25.2%) reckoned it to have tremendous clinical application and aided them in patient management. Nonetheless, as it is a recent technology, it has got a learning curve. Amongst the VRSI retina specialists, most were not confident of OCTA interpretation and depended upon their colleagues for interpretation. Similar to OCTA, widefield FA is also an emerging technology capable of imaging around 80% of retinal surface area.<sup>[21]</sup> More than two-third of the VRSI survey participants (78.5%) also believed widefield FA has advantageous over the conventional FA.

Macular edema secondary to retinal vein occlusions (RVO) is the second most important cause of visual impairment due to retinal vascular diseases.<sup>[22]</sup> Intravitreal anti-VEGF injections are a standard of care in such cases, which can be performed PRN with or without a loading dose.<sup>[23,24]</sup> Almost equal proportion of VRSI survey respondents elected to start PRN regimen from baseline (43.2%) and loading doses of three monthly injections, followed by PRN (40.2%), respectively, in the management of a fresh BRVO with CME. In a scenario when there is no response after three anti-VEGF injections and with significant capillary dropout on FA, more than half of the participants (53.3%) preferred to perform additional sectoral PRP. This was unlike the BVOS study recommendation of performing PRP only in case of development of retinal neovascularization.<sup>[25]</sup> The area of nonperfusion is not associated with functional outcomes or treatment burden in BRVO.<sup>[26]</sup> 28% of respondents preferred to switch to intravitreal steroids without performing PRP when there was no response to three anti-VEGF agents. This was very similar to the 2017 ASRS PAT survey, where in a similar case scenario, 29.7% participants opted to switch to intravitreal steroids (18.4% Dexamethasone, 11.3% Triamcinolone).<sup>[27]</sup>

The CVOS study recommended performing PRP once there is development of iris or angle neovascularization.<sup>[28]</sup> Later, intravitreal anti-VEGF injections have also been shown to cause regression of iris and retinal neovascularization ischemic retinal diseases.<sup>[29]</sup> In a situation where the patient has CRVO with early rubeosis and no CME, around 55.1% of participants opted to perform aggressive PRP with intravitreal anti-VEGF therapy, whereas a third of our respondents decided to perform only aggressive PRP.

Globally, DR and DME are a significant cause of visual loss amongst adults.<sup>[30]</sup> The DRCR.net Protocol S showed that the visual acuity was good and similar in both the Ranibizumab arm and the PRP arm at 5 years in the management of PDR.<sup>[31]</sup> Also, the ranibizumab arm had lower frequency of developing DME and visual field loss. The 12-month results of PROTEUS study showed that a combination of Ranibizumab with PRP was more effective than monotherapy alone for HR-PDR.<sup>[32]</sup> For treatment of a young 31-year-old diabetic man with PDR and no DME, the 2019 ASRS PAT survey respondents were in favor of doing a combination of anti-VEGF with PRP (37.7%) over PRP alone (29.3%).<sup>[20]</sup> However, in a similar case scenario of a 35-year-old diabetic man with PDR in one eye, very severe NPDR in the other eye and no DME in both eyes, more than half of the VRSI respondents preferred to perform PRP in both eyes (58.9%), whereas a minority preferred to perform PRP only in the eye with PDR. Only around 12.1% of respondents preferred to add an anti-VEGF to PRP.

The DRCR.net Protocol V has shown that patients with center-involving DME and good visual acuity can be managed by closely monitoring without treatment while maintaining good visual acuity.<sup>[33]</sup> A majority of the respondents opted for observation with good glycemic control with/without topical NSAIDs (61.7% [with NSAID] and 29.9% [without NSAID]). Only 8.4% decided to give an anti-VEGF injection in such a scenario.

The 2019 ASRS PAT survey showed that the majority of USA participants routinely use Bevacizumab as their first line of management in DME (65.8%) followed by Aflibercept (16.4%) and Ranibizumab (8.8%).<sup>[20]</sup> Surprisingly, Ranibizumab was the agent of choice in management of DME amongst the VRSI retinal specialists (46.7%). The Ranibizumab biosimilar, Razumab, which is approved by the regulatory authority in India for ocular use in 2015, was also selected by 20.6% of respondents as it is a valuable cost-effective option to Ranibizumab.<sup>[34]</sup> At the same time, Bevacizumab was preferred by 27.1% of participants, whereas Aflibercept was selected by only 4.7% of them. Here we note that almost two-third of the respondents would go for the Ranibizumab or its biosimilar as the first line agent in DME management. This selection pattern could be founded on the results of DRCT.net Protocol T, which showed that at the end of 2 years, all three anti-VEGF agents showed similar visual acuity outcomes in patients with better baseline visual acuity.<sup>[35]</sup> In patients with worse visual acuity at baseline, the superiority of Aflibercept over Ranibizumab seen at 1 year was no longer identified. However, higher Anti-Platelet Trialists' Collaboration (APTC) events were noted with Ranibizumab (12%) as compared to Aflibercept (8%) or Avastin (5%) (Global  $P = 0.047$ ). The participants were also questioned regarding any change in their management pattern and if they considered Aflibercept over Ranibizumab or Bevacizumab based on Protocol T outcomes. 60.7% of the respondents chose to start with Ranibizumab or Bevacizumab, and switch to Aflibercept only if there is poor response, whereas 13.1% preferred to use it over Ranibizumab or Bevacizumab in eyes with poor initial vision. Meta-analysis studies have shown a possible increase in risk of death and cerebrovascular accidents with use of anti-VEGF agents in DME.<sup>[36]</sup> In a case of 70-year-old woman with DME and recent history of stroke, when the participants were asked regarding the duration for which they would wait before administering anti-VEGF therapy, the participants responded as 2–3 months (18.7%), >6 months (11.2%) and 1 month (11.2%), respectively, whereas around 58.9% said that they would start with intravitreal steroids immediately. When the participants were questioned regarding the indications for starting with intravitreal steroid therapy for DME, more than half (50.5%) chose patients with pseudophakia and/or with a recent history of thromboembolic events. Moreover, 30.8% of participants do not start with intravitreal steroids unless there is a history of recent thromboembolic events. Although intravitreal dexamethasone implant (Ozurdex) was initially recommended every 6 monthly, real world data has shown it to last inside the eye for 3–5 months.<sup>[37]</sup> Even in the VRSI survey, when the participants were questioned regarding the duration of effect of Ozurdex implant, more than half of them chose 3 months (59.8%), followed by 2 months (19.6%), 4 months (15.9%) and 6 months (4.7%), respectively.

Earlier, laser photocoagulation was favored for management of DME, but with the advent of anti-VEGF agents, it is no

longer the standard of care.<sup>[38,39]</sup> In the VRSI survey, 22.4% of respondents routinely perform laser in DME, whereas a majority of them (68.2%) would do it only along with anti-VEGF therapy only when the edema is nonresolving after three anti-VEGF injections.

The DRCR.net Protocol U concluded that although adding Ozurdex to intravitreal Ranibizumab therapy does cause an anatomical improvement, but there is no significant change in the visual acuity in eyes with this combination therapy when compared to Ranibizumab monotherapy alone.<sup>[40]</sup> Nevertheless, in a scenario of unresponsive of DME to three doses of anti-VEGF injections in a pseudophakic patient, more than half of the VRSI survey respondents switch to an intravitreal steroid agent (54.2%), while another 28% perform a combination of focal laser with intravitreal steroids. Very few participants would switch to another anti-VEGF agent (6.5%) or combine focal laser with the anti-VEGF agent (6.5%). In sharp contrast, based on the 2019 ASRS PAT survey, 89.5% of respondents would switch to another anti-VEGF agent in absence of an adequate response to first-line anti-VEGF agent, whereas only 4.4% of them would switch to a steroid agent.<sup>[20]</sup> If they needed to switch between the anti-VEGF agents due to nonresponsive DME, more than half of the participants of the VRSI survey would do so after 3 injections (56.1%), whereas 15% would switch after 1–2 injections itself.

Clinical evaluation of a patient with DR is necessary to evaluate the stage of DR and to assess various clinical features.<sup>[38]</sup> In the past couple of decades, OCT has evolved as the single most important imaging modality in diagnosis and management of DME.<sup>[41]</sup> Features such as 'center-involving' and 'noncenter involving', and quantum of edema play a major role in determining the line of management.<sup>[42]</sup> When the participants were asked regarding their protocol for follow-up of DME patients, a majority of them revealed that they would perform clinical examinations at all visits and only advise OCT when needed (57%), whereas 41.1% respondents said that they would perform clinical examination with OCT at all visits.

The VRSI survey has shown that an equal number of retinal specialists (39.3%) prefer to start anti-VEGF therapy with either ranibizumab or bevacizumab. One interesting aspect from this questionnaire was that 19.6% of respondents preferred the ranibizumab biosimilar razumab as the first-line choice of anti-VEGF agent. Consequently, we note that more than half of them (58.9%) chose either ranibizumab or its biosimilar as the first line anti-VEGF agent. The practice of administering intravitreal injections in the operation theatre (OT) is dictated by several factors including availability of operation theatre time, associated extra cost, and perceived lower hygiene levels in the OPD.<sup>[43]</sup> Institutions where the injection load is high, have felt the need to create a semi sterile facility outside the operation theatres. In relation to the intravitreal injection practice pattern, a vast majority of the participants of the VRSI survey preferred an OT setup (90.7%), which could be either under an operating microscope (62.7%) or under direct (28%) visualization. Less than 10% performed the procedure in a semi-sterile setup such as minor OT.

This study represents the only national survey data on physicians' perceptions concerning medical and surgical retina topics in India. These practices are dynamic and can get altered with time based on growing evidence, wider availability and



accessibility to newer technologies and change in individuals' perception and acceptability to evolving management protocols. Unfortunately, the participation rate among Indian vitreoretinal specialists was small and data was obtained from only a minority of the VRSI's membership. This low participation rate limits the interpretation of results to  $\pm 8\%$ . Also, the lack of information regarding the training, experience and access to all treatment options of the participants in a drawback of our survey. For our future surveys, we would be formulating the questionnaire to incorporate these additional data. Moreover, we are trying to increase the response rate for future surveys.

This study, however, brings out the current practice in India, and compares it with the literature on RCTs as well as PAT survey. Some of our practice variations can be explained by the poor penetration of Health Insurance in our country, out of pocket expense for our patients, and varied socio-demographics. This can impact the treatment compliance and choice of anti-VEGF, including less usage of aflibercept and higher uptake of biosimilar ranibizumab.

## Conclusion

In conclusion, the VRSI practice patterns give us vital information regarding the investigational approaches, treatment preferences and follow-up preferences among Indian vitreoretinal specialists. This real-world information could be very important for the practitioners to formulate the optimal management strategy of vitreoretinal diseases with pragmatism.

## Financial support and sponsorship

Nil.

## Conflicts of interest

There are no conflicts of interest.

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## Supplemental Appendix 1

### Vitreoretinal Society of India Practice Pattern Survey 2020: Medical Retina Questionnaire

1. How long do you wait to perform a fluorescein angiography (FA) in a 35-year-old man with symptomatic central serous chorioretinopathy (CSCR) and visual acuity of 6/9?
  - a. At baseline
  - b. 1 month
  - c. 3 months
  - d. 6 months
2. How do you manage a 40-year-old man with symptomatic central serous chorioretinopathy (CSCR) with subfoveal leakage on fluorescein angiography (FA) and visual acuity of 6/12?
  - a. PDT—Standard Fluence
  - b. PDT—Reduced Fluence
  - c. Micropulse Laser
  - d. Oral therapy—eplerenone, rifampin, etc.
  - e. Intravitreal anti-VEGF therapy
  - f. Observe
3. How do you manage a 50-year-old man with symptomatic chronic CSCR, visual acuity of 6/18, OCT showing intraretinal cystoid spaces and serous macular detachment, no leakage on FA and no network on ICGA and OCTA?
  - a. PDT—Standard Fluence
  - b. PDT—Reduced Fluence
  - c. Micropulse Laser
  - d. Oral therapy—eplerenone, rifampin, etc.
  - e. Intravitreal anti-VEGF therapy
  - f. Observe
4. What is your treatment of choice for a patient with sub-foveal polypoidal choroidal vasculopathy (PCV)?
  - a. Baseline Anti-VEGF monotherapy
  - b. Baseline PDT + Anti-VEGF monotherapy
  - c. Baseline Anti-VEGF monotherapy, switch to other anti-VEGF agent if no response after three injections
  - d. Baseline Anti-VEGF monotherapy, add PDT if no response after three injections
  - e. Others
5. FLUID study reports that in neovascular AMD treated with treat and extend protocol; after resolution of intraretinal edema with treatment, a residual subretinal fluid which is less than 200  $\mu\text{m}$  at fovea can be observed with usual extension of reinjection time. How comfortable would you be to follow it in clinical practice?
  - a. I would agree with it
  - b. I would prefer complete resolution of subretinal fluid too
  - c. I do not follow treat and extend so cannot say
  - d. Do not know/not sure
6. Do you measure choroidal thickness in eyes with CSC?
  - a. Yes, I do it regularly
  - b. No, because it does not change my management
  - c. No, because I do not have access to OCT machine with choroidal imaging
  - d. I do not measure choroidal thickness, but I qualitatively evaluate the layers of choroid.
7. What is the most common indication for PDT in your clinical practice?
  - a. I do not do PDT
  - b. Nonresolving CNVM post anti-VEGF injections
  - c. Idiopathic polypoidal choroidal vasculopathy
  - d. Pachychoroid spectrum of disorders/pachychoroid neovascularopathy
8. Which statement best describes optical coherence tomography angiography (OCTA) in your retinal practice
  - a. I have access to OCTA and find it useful in my routine practice
  - b. I have access to OCTA, but do not find it useful in my routine practice
  - c. I do not have access to OCTA, but plan to purchase it in near future
  - d. I do not have access to OCTA, and do not plan to purchase it in the future
9. How confident are you in interpreting an OCTA for CNVM?
  - a. Very confident
  - b. Somewhat confident
  - c. Not confident and depend upon my colleagues for interpretation



10. What is your perception about the OCTA technology, compared to OCT?
- It is merely a research tool with no clinical application
  - It is a good research tool and has got limited clinical application
  - It is not a good research tool either as it has too many artefacts and does not change my patient management
  - It has tremendous clinical application and helps decide most of my patient management
11. Does the widefield FA have any advantage over the conventional FA?
- No, I can acquire similar peripheral images with the conventional FA
  - Yes, but it is an expensive technology to purchase
  - Yes, and I plan to purchase it in the near future
  - Not sure
12. A 60-year-old pseudophakic man with branch retinal vein occlusion (BRVO), visual acuity of 6/36, FA showing significant peripheral capillary dropout with nonresolving cystoid macular edema (CME) on OCT after three doses of anti-VEGF treatment. What is your next plan of action?
- Switch anti-VEGF agent without performing PRP
  - Switch to intravitreal steroid therapy without performing PRP
  - Sectoral PRP + Continue with same anti-VEGF agent
  - Sectoral PRP
  - Others
13. A 70-year-old woman with central retinal vein occlusion (CRVO), visual acuity of 6/18, resolved CME after anti-VEGF therapy has early rubeosis, no neovascularization of angles (NVA) and IOP of 14 mm Hg. What best describes your approach?
- Aggressive PRP only
  - Intravitreal anti-VEGF therapy only
  - Aggressive PRP + Intravitreal anti-VEGF therapy
  - Aggressive PRP + Intravitreal anti-VEGF therapy + Start on prophylactic anti-glaucoma medications
  - Others
14. What is your anti-VEGF treatment regimen for a 60-year-old phakic woman with fresh branch retinal vein occlusion (BRVO), visual acuity of 6/18 and cystoid edema on OCT?
- Loading dose of three monthly injections, followed by pro-re-nata (PRN)
  - PRN regimen from baseline
  - Treat-and-extend regimen
  - Others
15. How will you manage a 35-year-old type 1 diabetic man with early PDR in OD and very severe NPDR in OS with a dry macula in both eyes.
- Both eyes PRP
  - Both eyes PRP + Anti-VEGF injection therapy in OD
  - Both eyes PRP + Both Anti-VEGF injection
  - OD PRP and Observe OS
  - OD PRP + OD anti-VEGF injection therapy and Observe OS
16. A 54-year-old patient has moderate NPDR changes, with center-involving DME and CMT of 370  $\mu\text{m}$ , vision 6/6 in OD. HbA1c is 8.3%. What is your treatment strategy?
- Good glycemic control and repeat OCT after 4–6 weeks
  - Good glycemic control + Topical NSAID drops + Repeat OCT after 4–6 weeks
  - Start Intravitreal anti-VEGF injection therapy
  - Focal laser alone
  - Others
17. How frequently do you perform macular laser to diabetic macular edema (DME), along with anti-VEGF?
- I do in all cases
  - I do it in most cases
  - I do in nonresolving edema any time after 3 anti-VEGF injections
  - I do not do macular laser in DME
18. Which is your first line Anti-VEGF agent in your practice?
- Accentrix
  - Avastin
  - Eylea
  - Razumab

19. In which cases will you use intravitreal steroid as first line treatment for DME?
- In patients with recent thromboembolic events
  - In pseudophakic cases
  - a + b
  - I do not use intravitreal steroid as first line, except 'a'
20. How long do you feel the effect of Intravitreal Ozurdex last in DME?
- 2 months
  - 3 months
  - 4 months
  - 6 months
21. The head-to-head trial of aflibercept, ranibizumab and bevacizumab (Protocol T) concluded that aflibercept lead to more number of letters gained in eyes with poor initial vision and also had less adverse thromboembolic events in DME. Do you consider aflibercept over ranibizumab or bevacizumab?
- Yes, I prefer to use aflibercept in eyes with poor initial vision
  - No, aflibercept and ranibizumab had similar results at year 2
  - I start with bevacizumab or ranibizumab, but the switch to aflibercept if there is poor response.
  - I believe that all 3 drugs have similar effect
22. What is your anti-VEGF agent of choice in center-involving DME with visual acuity of 6/18?
- Intravitreal bevacizumab
  - Intravitreal aflibercept
  - Intravitreal ranibizumab (Accentrix)
  - Intravitreal ranibizumab (Razumab)
  - Intravitreal Ziv-aflibercept
23. How do you manage a pseudophakic patient with DME unresponsive to three doses of anti-VEGF injection?
- Switch anti-VEGF agent
  - Switch to intravitreal steroids
  - Focal laser + anti-VEGF therapy
  - Focal laser + intravitreal steroids
  - Others
24. For a nonresponsive DME, after how many injections do you switch the anti-VEGF agent?
- 1-2 injections
  - 3 injections
  - 4-6 injections
  - I do not switch between anti-VEGF injections
25. How do you follow-up a DME patient on long-standing anti-VEGF injection therapy?
- Perform OCT at all visits without clinical examination
  - Perform clinical examination and then OCT at all visits
  - Perform clinical examination at all visits and advise OCT when needed
  - Others
26. What best describes your intravitreal injection practice?
- I perform it in my OPD
  - I perform it in a semi-sterile set-up such as minor OT
  - I perform it in OT under direct visualization
  - I perform it in OT under microscopic visualization
27. A 70-year-old phakic woman has DME with a history of stroke. How long do you wait before administering anti-VEGF therapy?
- 1 month
  - 2-3 months
  - >6 months
  - I would immediately start with intravitreal steroids